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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,244	09/21/2001	Tony W. Ho	2560.0020000	4326
26111 7590 10/05/2007 STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C. 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			EXAMINER LANKFORD JR, LEON B	
			ART UNIT 1651	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/960,244

Applicant(s)

HO ET AL.

Examiner

Leon Lankford

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14, 19-21, 25 and 26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14, 19-21, 25 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Applicant's arguments have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 19-21 & 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has amended the claims to remove the limitation "greater than 91%" and by doing so is claiming a pure composition of the claimed cell phenotype. It is not clear that applicant has support in the instant specification for a pure population of the claimed phenotype therefore the amendment is considered to be new matter.

Further, the limitation "after 30 doublings" is considered to be new matter. Applicant points to support in the specification for this limitation however at the point of reference, the specification says after 50 doublings and there is no apparent support for the smaller range.

Prior art

A reconsideration of the instant application has led the examiner to believe that the cell population claimed are populations of MSC (mesenchymal stem cells) or mixed populations of MSCs and MAPCs. As better prior art has been found, the rejection over Furcht has not been maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14, 19-21 & 25-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Haynesworth et al. (1998, U.S. Patent 5,733,542) taken in light of Pittenger et al. (1999, *Science* 284: 143-147), Woodbury et al. (2000, *Journal of Neuroscience Research* 61: 364-370), and Lee et al. (2000, *Hepatology* 40: 1275-1284).

Haynesworth et al. teach a population of mesenchymal stem cells (MSCs) isolated from human adult bone marrow (Example 1; column 3, line 18, through column 4, line 51).

Pittenger et al. is cited as evidence that the MSCs of Haynesworth et al. can differentiate to various mesodermal cell lineages, including bone, cartilage, and adipose (Figure 2).

Woodbury et al. is cited as evidence that the MSCs of Haynesworth et al. can differentiate to neurons, (page 364, column 1, paragraph 1; page 365, column 2, paragraph 2, through page 367, column 2, paragraph 3).

Lee et al. is cited as evidence that the MSCs of Haynesworth et al. can differentiate to hepatocytes, (page 1277, column 1, paragraph 3; page 1279, column 1, paragraphs 2 and 3; Figure 2).

To invalidate a patent by anticipation, a prior art reference normally needs to disclose each and every limitation of the claim. See *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 953 F.2d 1360, 1369, 21 USPQ2d 1321, 1328 (Fed. Cir. 1991). However, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it. See *id.* and *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 630, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates. See *In re King*, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). **Inherency is not necessarily coterminous with the**

knowledge of those of ordinary skill in the art. See *Titanium Metals*, 778 F.2d at 780.

Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. See *id.* at 782. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. See *id.* at 782 ("Congress has not seen fit to permit the patenting of an old [composition], known to others..., by one who has discovered its...useful properties."); *Verdegaal Bros.*, 814 F.2d at 633.

This court's decision in *Titanium Metals* illustrates these principles. See *Titanium Metals*, 778 F.2d at 775. In *Titanium Metals*, the patent applicants sought a patent for a titanium alloy containing various ranges of nickel, molybdenum, iron, and titanium. The claims also required that the alloy be "characterized by good corrosion resistance in hot brine environments." *Titanium Metals*, 778 F.2d at 776. A prior art reference disclosed a titanium alloy falling within the claimed ranges, but did not disclose any corrosion-resistant properties. This court affirmed a decision of the PTO Board of Appeals finding the claimed invention unpatentable as anticipated. This court concluded that the claimed alloy was not novel, noting, "it is immaterial, on the issue of their novelty, what inherent properties the alloys have or whether these applicants discovered certain inherent properties." *Id.* at 782. This same reasoning holds true when it is not a property, but an ingredient, which is inherently contained in the prior art. The public remains free to make, use, or sell prior art compositions or processes, regardless

of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency, among other doctrines, enforces that basic principle." See *Atlas Powder Co. v. IRECO Inc.*, 51 USPQ2d 1943 (Fed. Cir. 1999).

Thus, a reference may be anticipatory if it discloses every limitation of the claimed invention either explicitly or inherently. A reference includes an inherent characteristic if that characteristic is the natural result flowing from the reference's explicitly explicated limitations. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

While the prior art does not clearly disclose all of applicant's claimed limitations, it would appear that the cells claimed are a population of MSCs as disclosed by Haynesworth. M.P.E.P. § 2112 reads, "The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." Something that is old does not become patentable upon the discovery of a new property, use, or application. Even if applicants had identified properties of the MSCs of Haynesworth et al. that Haynesworth et al. did not or could not test for, in this case the cells' telomerase expression level and ability to differentiate to various cell lineage types, such an identification would not render the MSCs of Haynesworth et al. patentable.

Claims 14, 19-21 & 25-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Haynesworth et al. taken in light of Jiang et al. (2002, *Nature* 418: 41-49). 14, 19-21 & 25-26

As discussed above, Haynesworth et al. teach a population of mesenchymal stem cells (MSCs) isolated from human adult bone marrow (Example 1; column 3, line 18, through column 4, line 51).

Jiang et al. is cited as evidence that Haynesworth et al.'s method of isolating their MSCs inherently yields a population that comprises mostly MSCs but also another rare cell type, MAPCs, that co-purify with the MSCs and that differentiate into mesodermal as well as ectodermal and endodermal cell lineages (Abstract; Figure 3). Jiang et al. teach that the MAPCs can undergo at least 100 population doublings (page 41, column 2, paragraph 1).

The above discussion of *Titanium Metals* and M.P.E.P. § 2112 also applies to this ground of rejection. In this case, the claims do not require that each and every cell in the population recited in claim 64 express telomerase and have the capacity to differentiate to cells of all three lineage types; indeed, the claims are drawn to an "isolated population" (*i.e.*, a population isolated from bone marrow) of cells, not to a population of isolated cells, each of which can differentiate into all three lineage types. Therefore, the claims read on the population of Haynesworth et al., which Jiang et al. teach inherently comprises a few MAPCs that have the claimed properties (page 41, column 1, paragraph 3). This ground of rejection might be overcome by an amendment to the

claims requiring that each cell in the population of claim 64 has the recited properties, not just that the population as a whole possesses the properties.

Even if applicants had identified properties of the MSC population of Haynesworth et al. that Haynesworth et al. did not test, in this case the presence of a rare cell type with the claimed properties that is inherently present in the MSC preparations of Haynesworth et al., such an identification would not render the MSC population of Haynesworth et al. patentable.

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not Applicants' cells differ and, if so, to what extent, from that discussed in the references. Therefore, with the showing of the references, the burden of establishing non-obviousness by objective evidence is shifted to Applicants. Significantly, applicant provides no factual evidence whatsoever to refute the holding of anticipation or obviousness. Note specifically that on the current record the only way of overcoming such a clear holding of anticipation is factual proof that the rejection is in error. *See* MPEP § 2112, disclosing that once a proper holding of anticipation is made, the burden shifts to applicant to demonstrate an unobvious difference between the claims and the prior art. *See also, In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) ("the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product"). Because applicant has not demonstrated any difference between the

claimed products and the prior art products, the rejection of record clearly must be maintained. Futher MPEP 2112 states:

[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on 'prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product - by - process claims. Quoting *In re Fitzgerald*, 619 F. 2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (itself quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 - 34 (CCPA 1977)).

Haynesworth in light of Pittenger, Woodley, Lee and Jiang (all as discussed above).

The teachings of the references are set forth above. It is the examiner's contention that the disclose properties which are not explicitly discussed in the prior art are inherent properties of the cells and cell populations disclosed in the Haynesworth reference, however if that is not the case it is apparent that the claimed characteristic of the cell population are a result of different culture conditions, or the ratio of MSCs to MAPC (as discussed in Jiang) or even the ratio of MSCs to an undetermined cell cellular "contaminant" thus effecting the population as a whole. It would appear that any actual differences between the cell population of Haynesworth and the claimed cell populations would be a question of the concentration of cells or the purity of the population. As such

even if the claimed populations are not anticipated by the Haynesworth populations, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.");< ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.).

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not Applicants' cells differ and, if so, to what extent, from that discussed in the references including the ability of the cell population to maintain its doubling rate. Therefore, with the showing of the references, the burden of establishing

non obvious by objective evidence is shifted to Applicants. Significantly, applicant provides no factual evidence whatsoever to refute the holding of anticipation or obviousness. Note specifically that on the current record the only way of overcoming such a clear holding of anticipation is factual proof that the rejection is in error. *See* MPEP § 2112, disclosing that once a proper holding of anticipation is made, the burden shifts to applicant to demonstrate an unobvious difference between the claims and the prior art. *See also, In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) ("the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product").

[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on 'prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product - by - process claims. Quoting *In re Fitzgerald*, 619 F. 2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (itself quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 - 34 (CCPA 1977)).

Accordingly, the claimed invention was at least prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14, 19-21 & 25-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14, 19-21 and 24-25 of copending Application No. 10/251685. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the same cell population wherein applicant has simply specified an inherent limitation in the instant case which is not claimed in the conflicting application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant argues (in '685) that the claimed cell population is distinct and unobvious over the population claimed in that application because of the limitation "induced to express" cardiac factors however this argument is not found persuasive. A transient phenotypic change, e.g. the induction of a transcription factor, does not preclude a holding of anticipation because it does not result in a material difference between the cells in question. A living cell's phenotype can change with something as simple as feeding the cell with a carbon source or providing an enzymatic cofactor but that does not change the identity of the cell *per se*. If a phenotypic change is merely the result of a culture method and not an actual change in the differentiation state or genotypic state of a cell then the cell *per se* has not become a new cell and it thus not novel over the cell before the culturing change. The examiner will illustrate his point with two disparate examples:

It is clear that if one induces a hematopoietic stem cell (HSC) to differentiate into an erythrocyte, the HSC and erythrocytes are distinct cells. The erythrocyte is genotypically and functionally different from the HSC and the change is not transient and not reversible.

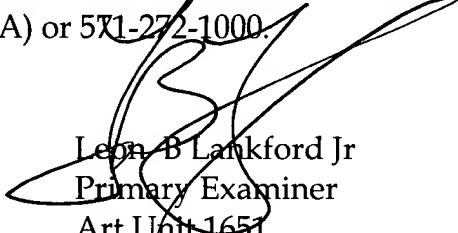
It is also clear that if an embryonic stem cell (ES) is exposed to LIF, it will not spontaneous differentiate into another cell variety of endothelial or epithelial origin but one would not consider the ES in solution with the LIF to be a different and distinct cell from the ES in a culture medium that doesn't contain LIF.

It is the examiner's contention that the instant scenario (the induction of transcription factors) is more akin to the second example (ES cells & LIF) and thus the cells *per se* would not be considered unobvious or even novel over the cells disclosed in the '244 application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Lankford whose telephone number is 571-272-0917. The examiner can normally be reached on Mon-Thu 7:30-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Leon B Lankford Jr
Primary Examiner
Art Unit 1651